

telephone on Tuesday, May 27, 2002, this listing of claims does not match the elected species, Group IV, as modified in the present Office Action on p. 3.

REMARKS

Claims 1-3 (in part), 5-6, 7-8 (in part), 11, and 22-25 are currently pending in the application.

35 U.S.C. § 103 Rejections (Obviousness)

All pending claims are rejected as unpatentable over Bechgaard et al. (US Patent No. 5,397,771). The Office Action states that Bechgaard et al. "teaches a method of administering a composition comprising diazepam [and] vegetable oil, [a] pharmaceutical composition [that] may also include alcohols," and a vehicle system which may increase "the possibility for designing a controlled release formulation...." See Office Action, p. 6, generally.

According to section 2142 of the Manual of Patent Examining Procedure (MPEP),

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

First, Bechgaard et al. does not teach all the claim limitations. The presently claimed invention requires subcutaneous (s.c.) administration to provide a peak plasma concentration within 4 hours *and* to achieve sustained delivery. Bechgaard specifically discloses nasal and intravenous administration, but does not mention the possibility of

subcutaneous administration. The Office Action asserts that although Bechgaard et al does not specifically teach s.c. administration, because Bechgaard et al. teaches optimization of the delivery system, it “would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the administer the composition of Bechgaard intravenously (sic – subcutaneously?).” See Office Action, top of p. 7.

Applicant respectfully submits that the claimed invention would not have been obvious to one of ordinary skill in the art. Bechgaard et al. specifically discloses nasal and intravenous administration routes, and stresses the surprising results using nasal administration wherein peak plasma concentrations are achieved nearly as fast as with intravenous administration (See Abstract). In particular, Bechgaard et al. states: “The *primary object* of the invention is to provide a pharmaceutical composition for the application of a biologically active substance *via a mucosal membrane* of a mammal, which composition is capable of producing a high plasma concentration of the pharmaceutically active substance *nearly as rapidly as by i.v. administration....*” See col. 3, lines 40-48, emphasis added). Nowhere does Bechgaard et al. suggest that one should veer away from the disclosed route of administration (nasal mucosal membrane) to try subcutaneous administration.

Second, although Bechgaard et al. does suggest optimizing the delivery system, (see col. 10, lines 21-29) this is entirely within the context of *a delivery system for mucosal membrane administration*. Nowhere in this paragraph is there a suggestion to actually *change* the route of administration. *Id.* In addition, although Bechgaard et al. also suggests that by combining solvents with the delivery system it “surprisingly increases the possibility for designing a controlled-release formulation which avoids peak

plasma concentrations" (see col. 10, lines 42-49), again, this is all within the context of "The vehicle system *according to the invention*...." – i.e. administration via a nasal mucosal membrane. *Id.*, line 42, emphasis added.

Third, Applicant respectfully submits that it is not obvious to change the route of administration to subcutaneous administration based on the teachings of Bechgaard, or based on the knowledge generally available to one of ordinary skill in the art. Subcutaneous administration is not a standard method of delivery for anti-convulsives, and using oil as the delivery vehicle for s.c. delivery is also non-standard. A silastic pellet or saline solution is a more typical delivery vehicle for subcutaneous delivery.

Moreover, as exemplified by the Bechgaard et al. patent, changing the route of administration for a pharmaceutical composition is not at all obvious - in general, whether changing the route to nasal mucosal membrane administration or to s.c. administration. The Bechgaard et al. patent is based on exactly that – a change in the route of administration, from i.v. to administration via the nasal mucosal membrane. There is nothing in the Bechgaard et al. patent, or in the knowledge generally available to one of ordinary skill in the art, that suggests changing the route of administration of an anti-convulsive to subcutaneous administration using an oil vehicle. Without a suggestion or motivation to make the change, such a change is not *prima facie* obvious.

In summary, the presently claimed invention requires subcutaneous administration of the lipophilic agent diazepam, in an oil vehicle, in the presence of benzyl alcohol, to achieve a peak plasma concentration within 4 hours and to achieve a sustained delivery. In contrast, the cited prior art, Bechgaard et al, discloses only i.v. and nasal administration, and specifically claims only nasal mucosal administration with peak

plasma concentration achieved within minutes. Therefore, the prior art does not disclose every element of the presently claimed invention; namely, subcutaneous administration and sustained delivery.

Further, the suggestion for how to achieve sustain delivery is directed solely within the context of nasal mucosal membrane delivery. There is no suggestion to change the route of administration to subcutaneous delivery to achieve the goal of sustained delivery, and it would not have been obvious to one having ordinary skill in the art to do so. Therefore, Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all pending claims are in condition for allowance. Reconsideration of the claims and a notice of allowance are therefore requested.

It is believed that no extension of time is needed; however, if an extension is required, this conditional petition for an extension of time is being made in the event that the need for an extension has been overlooked. Please charge deposit account number 19-4972 for any additional fees that may be required for the timely consideration of this
(continued over)

application.

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Respectfully submitted,

A handwritten signature in black ink, appearing to read "Keith J. Wood".

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